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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/670,914	09/24/2003	David W. Morris	20366-072001; PP023353.00	8849

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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

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12/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/670,914	MORRIS ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *61 and 73-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *61, 73-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of Group H, claims 54, 61, a method for detecting cancer, by detecting the level of a nucleic acid cited in tables 1-21, in the reply filed on 10/14/08 is acknowledged.

In a telephonic conversation, Applicant further elects colon cancer and the cDNA of SEQ ID NO:59.

The traversal is on the ground(s) that the search for more than one of groups would pose no serious burden to the Office.

This is not found persuasive because the searches for different groups are not coextensive, and it would be a serious burden to search all the groups together.

Applicant cancels claims 1-60, amends claim 61 and adds new claims 73-77.

Since applicant has elected Group H, a method for diagnosis of colon cancer, comprising detecting the level of SEQ ID NO:59, for action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, the embodiments of claims 61, 73-77, directed to: 1) a method for diagnosing a cancer, by detecting the expressed protein level, 2) a method for diagnosing a cancer, by detecting the level or expression of the genomic DNA SEQ ID NO:58, 3) a method for diagnosing of breast or prostate cancer, and 4) a method for detecting predisposition to a cancer have been withdrawn from consideration as being directed to a non-elected invention. See 37 C.F.R. 1.142(b) and M.P.E.P. 821.03. Claims 61, 73-77 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

1) A method for diagnosing cancer, by detecting the expressed protein level is distinct from the originally elected invention, because they use different reagents, and method steps. A nucleic acid and a protein are structurally distinct from each other, and require different method steps of detection, e.g, detection by nucleic acid hybridization, versus detection using an antibody to the protein.

2) A method for diagnosing cancer, by detecting the level or expression of the genomic DNA SEQ ID NO:58 is distinct from the originally elected invention, because the genomic DNA sequence of SEQ ID NO:58 is very large, of more than 10,000 nucleotides, as compared to SEQ ID NO:59 of 2245 nucleotides, and could express different mRNAs other than SEQ ID NO:59. Thus, SEQ ID NO:59 is **not a species**.

3) A method for diagnosing of breast or prostate cancer is distinct from the originally elected invention, because different target populations of cancer patients are used in the different methods.

4) A method for detecting predisposition to a cancer, as claimed in claims 73-76, is distinct from the originally elected invention, because different target populations of patients are used in the different methods. Those patients, who are used for detecting predisposition to a cancer, could be healthy individuals, which do not have symptom of a cancer, whereas those patients used for detecting of a cancer would already have or have symptom of a cancer. It is noted that claims 73-76 are reasonably interpreted as a method for diagnosis of colon cancer or of predisposition to colon cancer.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, Group H, claims 61, 73-77, a method for diagnosis of colon cancer, by detecting the level of SEQ ID NO:59 are examined in the instant application.

The embodiment of claims 61, 73-77 as drawn to: 1) a method for diagnosing a cancer, by detecting the expressed protein level, 2) a method for diagnosing a cancer, by detecting the level or expression of the genomic DNA SEQ ID NO:58, 3) a method for diagnosing of breast or prostate cancer, and 4) a method for detecting predisposition to a cancer have been withdrawn from consideration as being directed to a non-elected invention.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 61 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 61 is indefinite, for the use of the language "encoding", because it is commonly used in the art that a gene encodes a protein, but not a nucleic acid sequence.

Claim Rejections - 35 USC § 112, First Paragraph, Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 61, 73-77 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

To comply with the enablement requirement of 35 U.S.C. § 112, first paragraph, the specification must enable one skilled in the art to make and use the claimed invention without undue experimentation. The claims are evaluated for enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows: (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The specification discloses that cDNA sequences are screened for differential expression in cancer, using tumor tissue sample, including human colon cancer tissue and normal tissue, including non-cancerous prostate sample (Example 3 on page 138, Example 4 on page 142). **It is not clear that non-cancerous colon tissue is used in the specification.**

The specification, however, does not have any data or objective evidence that SEQ ID NO:59 is differentially expressed in colon cancer tissue as compared to non-cancerous colon tissue.

1. Claims 61, 73-77 are rejected under 112, first paragraph, for lack of enablement for a method for **diagnosis of colon cancer.**

In the absence of objective evidence, one cannot determine whether the nucleic acid of SEQ ID NO: 59 is differentially expressed in colon cancer tissues as compared to non-cancerous colon tissues, because the level of expression of a nucleic acid in cancer tissue is not predictable. It is well known in the art that not every gene in a cancer cell is affected in carcinogenesis, such as mutation or changes in expression as compared to normal control cells. For example, Stanton, P et al, 1994, Br J Cancer, 70: 427-433 teach that the level of expression of epidermal growth factor receptor (EGFR) cannot be predicted from cell lines or tumors (p.432, second column, last paragraph), and that from ten tumors from which the cell lines are derived, only two of the tumors display elevated levels of EGFR, BICR6 and BICR18 proteins (table V on page 430, and first column, last paragraph of page 430) In other words, not only the level EGFR, BICR6 and BICR18 proteins are the same as normal control in 8 tumors, the rest of other proteins in table V are not different from normal control in all ten tumors. Similarly, Iehle, C et al, 1999, J Steroid Biochem Mol Biol, 68: 189-195, teach that although the level of 5-alpha-reductase-1 is increased in prostate cancer tissue, the level of the isoform 5-alpha-reductase-2 is the same as that of normal prostate (abstract). Abbaszadegan, M R, et al, 1994, Cancer Res, 54: 4676-4679, teach that the level of multidrug resistance-associated protein (MRP) detected in malignant hematopoietic cells is similar to the level found in normal hematopoietic cells (p.4678, second column, last 6 lines of second paragraph).

Further, since it is not clear what constitutes a "**normal control**", as recited in claims 61, 73, 76, which is not necessarily a non-cancerous colon tissue, one would not know how to use the claimed method. Similarly, it is not clear what constitutes the **non-cancerous colon control**, as claimed in claim 77, which is not necessarily non-cancerous colon tissue. The level of SEQ ID

NO:59 in the claimed non-cancerous control is not predictable, because the level of a nucleic acid in a tissue is not predictable. In view of the above, one would not know how to use the claimed method.

In addition, the claimed method, as claimed in claim 77, would be non-specific, because a **complement** could be a full or partial complement, wherein the partial complement of SEQ ID NO:59 needs to share with SEQ ID NO:59 only a few complementary nucleotides.

Further, a **difference,** as recited in claims 61, 73, 76, 77, encompasses either an increase or a decrease. One cannot predict which one of the results, an increase or a decrease in the level of SEQ ID NO:59 in colon cancer tissue as compared to non-cancerous colon tissue.

2. Claims 73-76 are also rejected under 112, first paragraph, for lack of enablement for a method for diagnosis of colon cancer, using a sequence **at least 95% or 98% identical to SEQ ID NO:59.**

Even if SEQ ID NO: 59 were overexpressed in colon cancer tissue as compared to non-cancerous colon tissue, one cannot predict that a sequence at least 95% or 98% identical to SEQ ID NO:59 could be used for diagnosis of colon cancer. It is unpredictable that the 95% or 98% variants of SEQ ID NO:59 would be differentially expressed in colon cancer tissue as compared to the non-cancerous colon control tissue. It is well known in the art that variants of a sequence do not necessarily express at the same level as the corresponding wild type. For example, Schmid S et al, 2001 (J comparative Neurology, 430(2): 160-71), teach that the variants flip/flop of the gene GluR are expressed at higher levels in neurons in the auditory braistem, as compared to the wild type GluR-A and GluR-B, and that neurons in the central nucleus of the inferior collicullus express high levels of GluR-B flip but only low levels of the other receptor subunits.

Conner et al, 1996 (Mol Brain Res, 42: 1-17), teach that full length trkB is found the hippocampus in patients with Alzheimer's disease, but not in hippocampi of either normal age-matched individual or patients with Huntington's disease, and that truncated trkB is found in senile plaques in hippocampus and temporal lobe in both patients with Alzheimer's disease and Huntington's disease, but not in normal brains of aged-matched individuals (page 8, item 3.1.2).

MPEP 2164.03 teaches that "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature ot the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling."

Given the above unpredictability, and in view of the complex nature of the invention, a lack of sufficient disclosure in the specification, and little is known in the art concerning the claimed invention, there would be an undue quantity of experimentation required for one of skill in the art to practice the claimed invention, that is commensurate in scope of the claims.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, LARRY HELMS can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH-TAM DAVIS
December 11, 2008

/Larry R. Helms/

Acting SPE of Art Unit 1643